United States Court of Appeals for the Federal Circuit

AJINOMOTO CO., INC., AJINOMOTO HEARTLAND INC.,
Appellants

v.

INTERNATIONAL TRADE COMMISSION,
Appellee

CJ CHEILJEDANG CORP., CJ AMERICA, INC., PT CHEILJEDANG INDONESIA,
Intervenors

CJ CHEILJEDANG CORP., CJ AMERICA, INC., PT CHEILJEDANG INDONESIA,
Appellants

v.

INTERNATIONAL TRADE COMMISSION,
Appellee

AJINOMOTO CO., INC., AJINOMOTO HEARTLAND INC.,
Intervenors

2018-1590, 2018-1629

Appeals from the United States International Trade Commission in Investigation No. 337-TA-1005.

Decided: August 6, 2019

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Before DYK, MOORE, and TARANTO, *Circuit Judges.*

Opinion for the court filed by *Circuit Judge* TARANTO.

Opinion concurring in part and dissenting in part filed by *Circuit Judge* DYK.

TARANTO, *Circuit Judge.*

Ajinomoto Co., Inc. and Ajinomoto Heartland Inc. (collectively, Ajinomoto) filed a complaint against CJ CheilJedang Corp., CJ America, Inc., and PT CheilJedang Indonesia (collectively, CJ) with the International Trade Commission, alleging that CJ was importing certain

products that infringed Ajinomoto's U.S. Patent No. 7,666,655. CJ used several strains of *Escherichia coli* bacteria to produce L-tryptophan products, which it then imported into the United States. The Commission determined that CJ's earlier strains did not infringe but that CJ's two later strains did. The Commission also found that the relevant claim of the '655 patent is not invalid for lack of an adequate written description.

Ajinomoto appeals the Commission's claim construction underlying the determination of no infringement by the earlier strains. CJ cross-appeals aspects of the determination of infringement by the later strains and the rejection of the invalidity challenge. We affirm.

I

A

The '655 patent claims *E. coli* bacteria that have been genetically engineered to increase their production of aromatic L-amino acids, such as L-tryptophan, during fermentation, as well as methods of producing aromatic L-amino acids using such bacteria. *See* '655 patent, col. 2, lines 40–45. In particular, the '655 patent identifies a specific gene in the *E. coli* genome, the *yddG* gene, that encodes a membrane protein, the YddG protein. *Id.*, col. 2, lines 46–48. That protein transports aromatic L-amino acids out of the bacterial cell and into the surrounding culture medium, where they can be collected. *See id.*, col. 7, lines 11–16. When *yddG* gene activity in bacteria is enhanced so that more YddG protein is produced, the bacteria show increased production of, and increased resistance to, aromatic L-amino acids. *Id.*, col. 2, lines 49–57.[1]

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[1] The specification defines a bacterium's "resistance" to an amino acid as its ability "to grow on a minimal medium containing" the amino acid on "which unmodified or

The ’655 patent describes three ways to enhance the activity of the *yddG* gene. First, plasmids containing additional copies of the *yddG* gene can be introduced into the bacterium. *Id.*, col. 2, lines 50–52; *id.*, col. 5, line 62, through col. 6, line 2. Second, additional copies of the *yddG* gene can be inserted into the bacterial chromosome. *Id.*, col. 2, lines 52–54; *id.*, col. 6, lines 3–6. Third, a stronger “promoter” than the one native to the *E. coli yddG* gene can be used. *Id.*, col. 2, lines 54–57; *id.*, col. 6, lines 12–15.[2]

Claim 20, the only claim of the ’655 patent still asserted when the Commission issued its decision, claims “[a] method for producing an aromatic L-amino acid, which comprises cultivating the bacterium ***according to any one of*** claims 9–12, 13, 14, 15–18, or 19.” *Id.*, col. 24, lines

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the wild type, or the parental strain of the bacterium cannot grow,” or its ability “to grow faster” on such a medium “than unmodified or the wild type, or the parental strain of the bacterium.” ’655 patent, col. 4, lines 49–56.

[2] A promoter is a nucleotide sequence within a DNA molecule, located adjacent to the nucleotide sequence that constitutes the gene to be expressed. The Lewin textbook cited by Ajinomoto shows a “typical promoter” around 41 nucleotides long. J.A. 6043; *see also* J.A. 6177 (article by Deuschle et al., cited at ’655 patent, col. 6, lines 18–21, showing longer promoters). The promoter is the binding site for RNA polymerase, which initiates transcription (the first step in gene expression) by separating the two strands of DNA. The ’655 patent’s specification defines “[s]trength of promoter” with reference to the “frequency of acts of the RNA synthesis initiation.” ’655 patent, col. 6, lines 15–16.

The promoter is only one part of a gene’s “expression regulation sequence,” which controls expression of the gene. *See id.*, col. 3, line 14; *id.*, col. 5, line 2. Besides promoters, the “expression regulation sequence” can include, *e.g.*, operators, enhancers, terminators, and silencers.

4–6 (emphasis added). Of the claims in that list, claims 9 and 15 are the independent claims, and they are the two alternatives, under claim 20, of importance in this case.

Claim 9 recites:

> 9. A recombinant *Escherichia coli* bacterium, which has the ability to accumulate aromatic L-amino acid in a medium, wherein the aromatic L-amino acid production by said bacterium is enhanced by enhancing activity of a protein in a cell of said bacterium beyond the levels observed in a wild-type of said bacterium,
>
> **[1]** and in which said protein consists of the amino acid sequence of SEQ ID NO: 2
>
> **[2]** and said protein has the activity to make the bacterium resistant to L-phenylalanine, fluoro-phenylalanine or 5[-]fluoro-DL-tryptophan,
>
> **[3]** wherein the activity of the protein is enhanced by **[3a]** transformation of the bacterium with a DNA encoding the protein to express the protein in the bacterium, **[3b]** by replacing the native promoter which precedes the DNA on the chromosome of the bacterium with a more potent promoter, **[3c]** or by introduction of multiple copies of the DNA encoding said protein into the chromosome of said bacterium to express the protein in said bacterium.

Id., col. 22, lines 51–67 (paragraph breaks and bold numbering added). The Commission referred to limitation [1] as the "protein limitation," limitation [2] as the "resistance limitation," and limitation [3] as the "enhancement limitation." Claim 15 is materially identical to claim 9, except for the protein limitation. Whereas claim 9 identifies the claimed protein by a specific amino-acid sequence, claim 15 identifies it by reference to a corresponding DNA sequence—a protein "encoded by the nucleotide sequence

which hybridizes with the complement of the nucleotide sequence of SEQ ID NO: 1 under" certain conditions. *See id.*, col. 23, lines 14–32.

B

In May 2016, Ajinomoto filed a complaint against CJ with the Commission under 19 U.S.C. § 1337. Ajinomoto alleged that CJ violated § 1337(a)(1)(B)(ii) by importing animal-feed-grade L-tryptophan products produced by a process covered by the '655 patent.[3] The Commission instituted an investigation based on Ajinomoto's complaint.

The parties before us, including the Commission, agree that whether the accused products were produced by a process covered by the patent is a question of infringement. The proceeding focused on three groups of *E. coli* strains that CJ has used to produce tryptophan. First, CJ's "earlier strains" contained both the native *E. coli yddG* gene and the native *E. coli yddG* promoter, except that the first nucleotide of the promoter was changed through chemical mutagenesis, resulting in a stronger promoter. Second, in November 2016, several months after Ajinomoto filed its complaint, CJ began using its first "later strain," which contained two copies of a *yddG* gene: (1) the native *E. coli yddG* gene with the native *E. coli yddG* promoter; and (2) a non-*E. coli yddG* gene with two promoters—(2a) a native non-*E. coli yddG* promoter and (2b) an *rmf* promoter.[4] Third, in December 2016, CJ started using its second "later

[3] Ajinomoto also alleged that CJ infringed U.S. Patent No. 6,180,373, which similarly claims methods of producing tryptophan using genetically engineered bacteria. The '373 patent expired on January 30, 2018, and is not at issue in this court.

[4] The *rmf* and *rhtB* promoters are promoters associated with other genes in the *E. coli* genome.

strain," which also contained two copies of a *yddG* gene: (1) the native *E. coli yddG* gene with the native *E. coli yddG* promoter; and (2) a codon-randomized non-*E. coli yddG* gene with two promoters—(2a) an *rmf* promoter and (2b) an *rhtB* promoter.[5]

In August 2017, the administrative law judge (ALJ) issued a final initial determination. The ALJ construed "replacing the native promoter . . . with a more potent promoter" in the enhancement limitation to mean "removing the native upstream region of the *yddG* gene and inserting one of a class of promoters that controls expression of a different gene." J.A. 90–91. Using that construction, the ALJ found that CJ's earlier strains did not infringe; he found that they failed to meet the enhancement limitation because CJ created the more potent promoter in those strains by mutagenesis of a single nucleotide rather than removal of the entire native promoter and insertion of a new promoter. As to CJ's later strains, the ALJ found that (a) the first later strain did not infringe because Ajinomoto had failed to prove that it met the resistance limitation, and (b) the second later strain also did not infringe because

[5] Each particular codon (three nucleotides in a row on a DNA molecule) that encodes for an amino acid always encodes for the same amino acid, but many of the 20 amino acids are encoded by more than one of the 64 codons. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1208 n.4 (Fed. Cir. 1991) (discussing "redundancy" of genetic code). For instance, the DNA sequences TTA and TTG both code for the amino acid leucine. "Codon randomization" refers to creation of DNA molecules that use different codons (*e.g.*, TTA or TTG) to code for the same amino acid (*e.g.*, leucine) in building the same protein. *See Mycogen Plant Sci. v. Monsanto Co.*, 243 F.3d 1316, 1323 (Fed. Cir. 2001) ("[O]ne codon can be substituted for another in the gene without changing the amino acid and resulting protein.").

its non-*E. coli* YddG protein was not equivalent to the claimed *E. coli* YddG protein under the doctrine of equivalents. Finally, the ALJ found that claim 20 of the ’655 patent is invalid for lack of an adequate written description of the “more potent promoter” limitation incorporated into that claim.

In October 2017, the full Commission decided to review the ALJ’s final initial determination in its entirety, and in December 2017, the Commission issued its decision. It affirmed the ALJ’s construction of “replacing the native promoter . . . with a more potent promoter” and accordingly affirmed the ALJ’s finding that CJ’s earlier strains did not infringe. But the Commission reversed several of the ALJ’s other findings. Specifically, it determined that both of CJ’s later strains met all disputed claim limitations and thus infringed claim 20 and that claim 20 was not proved to lack an adequate written description. The Commission accordingly entered a limited exclusion order against CJ’s infringing products, *i.e.*, those made by both of CJ’s later strains but not its earlier strains. The Commission also issued a cease-and-desist order against CJ America, which held inventory of the infringing products.

Ajinomoto and CJ both timely appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(6).

II

We begin with Ajinomoto’s appeal of the Commission’s finding of no infringement by the earlier strains. Ajinomoto challenges that finding solely by arguing that the Commission erred in its claim construction of “replacing the native promoter . . . with a more potent promoter.” Ajinomoto argues that, properly construed, the phrase is not limited to removing the entire native promoter and inserting a new promoter, as the Commission concluded, but encompasses mutagenesis of individual nucleotides within the native promoter. We review the Commission’s claim construction de novo, as the Commission relied on only

intrinsic evidence and made no factual findings based on extrinsic evidence. *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 841 (2015); *see Cont'l Circuits LLC v. Intel Corp.*, 915 F.3d 788, 795 (Fed. Cir. 2019). We agree with the Commission's claim construction and therefore affirm the non-infringement finding.

The ordinary and customary meaning of the claim language provides support for the Commission's claim construction. The language of "replacing the native promoter . . . with a more potent promoter" suggests, in ordinary parlance, an operation at the level of the entire promoter as a unit, not at the level of a single nucleotide that is just one small component of the promoter. To say that one is "replacing" an object (*e.g.*, a laptop computer, a bicycle, a sailboat, a blender) suggests that one is doing more than altering one small part of it. That suggestion is bolstered when one also uses language (here, a "more potent promoter") referring to the replacement at the level of the overall object. The suggestion is further reinforced by the most apt of the dictionary definitions of "replace" introduced before the Commission—"to provide a substitute for." J.A. 10361; *see also* J.A. 5622 (patent applicants explaining "replacing" as "substitut[ing]"). In many contexts, one would not refer to swapping out one small component of a larger unit as "replacing" the unit or as providing a "substitute" for the unit, even though the net result is a differently constituted larger unit. Context matters, of course, but here, Ajinomoto has not shown a contrary common understanding (or even one of several common understandings) among relevant artisans in the specific context of replacing a promoter with a more potent promoter. Accordingly, the claim language, though hardly establishing a plain meaning, supports the Commission's construction.

The specification offers additional support, though it too is hardly plain insofar as it bears on the particular construction issue. The specification states that "the enhancement of gene expression can be achieved by locating the

DNA of the present invention under control of more potent promoter instead of the native promoter." '655 patent, col. 6, lines 12–15. That statement speaks of a promoter as a unit, but it does not use the language of "replacing." Indeed, the specification nowhere uses that language. But it does discuss "substituting" promoters, using a term that, as indicated above, is an apt definition of "replacing" here. The specification describes "[t]he present inventions" as including "[t]he bacterium according to the above bacterium, wherein native promoter of said DNA is substituted with more potent promoter." *Id.*, col. 3, lines 19–21. The term is then used in Example 4, which is titled "Substitution of the Native Upstream Region of yddG Gene by the Hybrid Regulatory Element Carrying the P_L Promoter and SD_{lacZ} in *E. coli* Chromosome," and which involves removing the entire native promoter and inserting a new promoter. *See id.*, col. 11, line 5, through col. 12, line 46. The sole specification example of "substitution" thus fits the Commission's claim construction. And while the specification discusses mutagenesis, it does so only in the context of the protein-coding region of the *yddG* gene, not the promoter. *See id.*, col. 5, lines 18–30.

We turn finally to the prosecution history—on which the parties to this case have focused most of their competing analyses. We conclude that the best understanding of what transpired before the examiner further supports the Commission's construction. Because the prosecution history reinforces what is already suggested by the claim language and specification, this case provides no occasion, contrary to Ajinomoto's contention (Ajinomoto Br. 34), for requiring clear and unmistakable disavowal or disclaimer to justify a claim construction contrary to a meaning evident from the claim language and specification.

What was claim 2 of the original application recited "[t]he bacterium according to claim 1, wherein said activities of proteins . . . is enhanced by transformation of said bacterium with DNA coding for the protein . . . *or by*

alteration of expression regulation sequence of said DNA on the chromosome of the bacterium." J.A. 5047 (emphasis added).[6] The examiner rejected the claim for lack of an adequate written description and lack of enablement. As to written description, the examiner explained that "[w]hile generic expression regulation sequences are known in the art, a particular, endogenous expression regulation sequence for the DNA that encodes [amino-acid] SEQ ID NO:2, or related sequences, is not described." J.A. 5371. "Without description of the endogenous regulation sequence," the examiner continued, "an endogenous regulation sequence that has been altered to increase expression of said protein also lacks adequate written description." *Id.* Turning to enablement, the examiner stated:

> The specification, while being enabling for *Escherichia* strains wherein the native promoter for the DNA encoding SEQ ID NO: 2 has been changed by substitution with a more potent promoter, does not reasonably provide enablement for the genus of an L-amino acid producing bacterium wherein the activity of proteins described by SEQ ID NO: 2 and related sequences is increased due to specific alterations within the chromosomal expression regulation sequence for DNA encoding said proteins.
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> . . . .

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[6] Although claims 9 and 15 issued from what were numbered as claims 12 and 24 when added during prosecution, the parties do not dispute that the amendments to original claim 2 (which eventually was cancelled) are relevant to construing issued claims 9 and 15. The same "replacing the native promoter . . . with a more potent promoter" language added to original claim 2 was eventually added to claims 9 and 15.

> The instant specification teaches how to select *Escherichia* bacteria that have an increased production of L-amino acids, and the art teaches how to mutagenize chromosomal DNA and how to characterize the mutations in the DNA. However, neither the specification nor the art contain any examples of how to specifically change endogenous *Escherichia* chromosomal expression regulation sequences for the DNA encoding proteins described by SEQ ID NO: 2, or related sequences, such that the activity of said proteins in the bacteria is increased. The art and the specification provide enablement for inserting a known promoter in the chromosomal DNA to upregulate the expression of the DNA encoding SEQ ID NO: 2; however, neither the specification nor the art enable making specific changes to expression regulation sequences for DNA encoding SEQ ID NO:2 and related sequences on the chromosome of *Escherichia* bacteria. The art and specification lack a detailed description of the structure of the instant endogenous expression regulation sequences, and they lack any guidance on how to alter such sequences such that DNA expression is increased; therefore, to make the instant bacteria with altered expression regulation sequences would be unpredictable.

J.A. 5374–75.

In response to the rejections, the applicants amended the claim to recite "replacing the native promoter that precedes a DNA encoding said protein . . . with a more potent promoter" instead of "by alteration of expression regulation sequence of said DNA." J.A. 5610. The applicants explained the amendment as follows: "Applicants have amended Claim 2 consistent with the Examiner's recognition that the specification enables Escherichia strains wherein the native promoter for the DNA encoding SEQ ID

NO: 2 has been changed by substitution with a more potent promoter." J.A. 5622.

Reading the written-description and enablement rejections together, we think that the most reasonable understanding of the examiner's comments is that the examiner was drawing a distinction between alterations to the promoter, which were sufficiently described and enabled because *E. coli* promoters were well understood in the art, and alterations to the expression-regulation sequence more broadly, which were not adequately described or enabled. To be sure, the examiner's statement that the art and the specification "lack any guidance on how to alter such sequences such that DNA expression is increased" might at first suggest that the applicants had not described and enabled the full scope of "alteration." But in context, this statement is best read as meaning that the applicants had not described and enabled the full scope of "expression regulation sequence," so that "alteration" of that sequence also was not adequately described or enabled, even though general techniques for altering DNA sequences were well known in the relevant art.

We need not determine the precise basis for the examiner's rejections, however, as "there is no principle of patent law that the scope of a surrender of subject matter during prosecution is limited to what is absolutely necessary to avoid a prior art reference that was the basis for an examiner's rejection." *Norian Corp. v. Stryker Corp.*, 432 F.3d 1356, 1361 (Fed. Cir. 2005). Rather, patentees frequently "surrender more through amendment than may have been absolutely necessary to avoid particular prior art." *Id.* That principle logically extends to amendments made to overcome rejections under § 112. *Cf. Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1095–96 (Fed. Cir. 2013). Indeed, we have stated more generally that "[t]he question is what a person of ordinary skill would understand the patentee to have disclaimed during prosecution, not what a person of ordinary skill would think the

patentee needed to disclaim during prosecution." *Tech. Props. Ltd. LLC v. Huawei Techs. Co.*, 849 F.3d 1349, 1359 (Fed. Cir. 2017). A patentee must "be held to what he declares during the prosecution of his patent," because a contrary rule would undermine "[t]he public notice function of a patent." *Springs Window Fashions LP v. Novo Indus., L.P.*, 323 F.3d 989, 995 (Fed. Cir. 2003).

We conclude that this is a case where the applicants surrendered more than may have been necessary. As discussed above, the best reading of the prosecution history is that, to overcome the written-description and enablement rejections, it might well have sufficed if the applicants had narrowed their claims from alterations to the overall expression-regulation sequence to alterations to the promoter. But the applicants did not merely change "expression regulation sequence" to "native promoter"; they also changed "alteration" to "replacing." Just as "when different words are used in separate claims, they are presumed to have different meanings," *Aspex Eyewear, Inc. v. Marchon Eyewear, Inc.*, 672 F.3d 1335, 1349 (Fed. Cir. 2012), when a word is changed during prosecution, the change tends to suggest that the new word differs in meaning in some way from the original word.

That inference is bolstered by the applicants' remarks accompanying the amendment. Those remarks effectively equate "replacing the native promoter . . . with a more potent promoter" in the amended claim with "chang[ing]" the native promoter "by substitution with a more potent promoter." J.A. 5622. As we have already noted, Example 4, described as involving "substitution" of a promoter, involves removal of the entire native promoter and insertion of a new promoter. '665 patent, col. 11, line 5, through col. 12, line 46. The applicants' remarks, understood in light of the word choices and the specification, thus reinforce the Commission's conclusion that the new claim language does not include mutagenesis of individual nucleotides.

For those reasons, we affirm the Commission's claim construction and its finding that CJ's earlier strains do not infringe based on that claim construction.

III

CJ, in its cross-appeal, challenges the Commission's determinations that CJ's second later strain met the protein limitation, that both of CJ's later strains met the resistance limitation, and that claim 20 is not invalid for lack of an adequate written description. We affirm the Commission as to all three issues.

A determination of infringement or non-infringement, whether literal or under the doctrine of equivalents, is a finding of fact, reviewed here for substantial evidence. *Kinik Co. v. Int'l Trade Comm'n*, 362 F.3d 1359, 1361 (Fed. Cir. 2004). But a determination of the applicability or inapplicability of prosecution history estoppel, which limits the availability of the doctrine of equivalents, is a matter of law, reviewed de novo. *Spectrum Pharm., Inc. v. Sandoz Inc.*, 802 F.3d 1326, 1337 (Fed. Cir. 2015). The determination that a patent claim did not lack adequate support in the written description is a factual finding, reviewed for substantial evidence. *Rivera v. Int'l Trade Comm'n*, 857 F.3d 1315, 1319 (Fed. Cir. 2017). Ajinomoto had to prove infringement by a preponderance of the evidence, while CJ had to prove invalidity by clear and convincing evidence. *See Motorola Mobility, LLC v. Int'l Trade Comm'n*, 737 F.3d 1345, 1348 (Fed. Cir. 2013); *Enercon GmbH v. Int'l Trade Comm'n*, 151 F.3d 1376, 1384 (Fed. Cir. 1998).

A

The Commission found that CJ's second later strain infringed claim 20, which covers two alternatives of relevance in this case—the claim 9 alternative and the claim 15 alternative. The infringement finding for CJ's second later strain does not rest on the claim 15 alternative, which, in its protein limitation, requires a protein encoded

by a nucleotide sequence that hybridizes with the complement of SEQ ID NO:1 (the nucleotide sequence of the *E. coli yddG* gene). The Commission did not find, and Ajinomoto does not argue for, either literal or equivalents infringement based on claim 15. The Commission found infringement under the claim 9 alternative—specifically, it found that the YddG protein encoded by the codon-randomized non-*E. coli yddG* gene of this strain is an equivalent of SEQ ID NO:2 (the amino-acid sequence of the *E. coli* YddG protein), as required by the protein limitation of claim 9.

CJ challenges that finding on two grounds. Based on an amendment to original claims made during prosecution, CJ asserts that prosecution history estoppel bars Ajinomoto from relying on the doctrine of equivalents to meet the protein limitation. Separately, CJ asserts that the non-*E. coli* YddG protein of CJ's second later strain cannot reasonably be found to be an equivalent of the claimed *E. coli* YddG protein under the function-way-result test for equivalence. We address those arguments in turn.

1

Under the doctrine of prosecution history estoppel, "[a] patentee's decision to narrow his claims through amendment may be presumed to be a general disclaimer of the territory between the original claim and the amended claim." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 740 (2002). The Supreme Court has specified three ways the patentee can rebut that presumption, each of which, if established, means that "the amendment cannot reasonably be viewed as surrendering a particular equivalent." *Id.* First, "[t]he equivalent may have been unforeseeable at the time of the application." *Id.* Second, "the rationale underlying the amendment may bear no more than a tangential relation to the equivalent in question." *Id.* Third, "there may be some other reason suggesting that the patentee could not reasonably be

expected to have described the insubstantial substitute in question." *Id.* at 740–41.

In this case, the relevant facts about what transpired during prosecution are as follows. Claim 1 as originally filed recited two alternative conditions for the claimed protein:

> a protein as defined in the following (A) or (B) in a cell of said bacterium:
>
> (A) a protein which comprises the amino acid sequence shown in SEQ ID NO:2 in Sequence listing;
>
> (B) a protein which comprises an amino acid sequence including deletion, substitution, insertion or addition of one or several amino acids in the amino acid sequence shown in SEQ ID NO:2 in Sequence listing.

J.A. 5047. The examiner rejected that claim as anticipated by a reference disclosing the *E. coli* "*yfiK* gene product" (*i.e.*, the *E. coli* YfiK protein)—which differed from SEQ ID NO:2 by deletion, substitution, insertion, or addition of several amino acids and, therefore, did not come within the (A) alternative but did come within the (B) alternative. J.A. 5378. In response, the applicants left the (A) alternative alone but replaced the language following (B) with new language: "a protein which comprises an amino acid sequence that is encoded by a nucleotide sequence that hybridizes with the nucleotide sequence of SEQ ID NO:1 under stringent conditions." J.A. 5609.[7]

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[7] As previously noted, claims 9 and 15 issued from new claims added at the same time as this amendment. *See supra* note 6. Claims 9 and 15 respectively contain the same language as the (A) and (B) limitations in claim 1 after it was amended. Claim 20, the claim at issue, treats

As an initial matter, CJ's argument for prosecution history estoppel in this case involves an unusual circumstance. The infringement determination does not rest on finding an equivalent of the new claim language—namely, the (nucleotide) SEQ ID NO:1 language now in claim 15. Rather, it rests on finding an equivalent of the (amino-acid) SEQ ID NO:2 language now in claim 9, which was not itself altered by the amendment at issue. That is, the original claim provided two alternatives; only the second was modified by amendment; and only the first is asserted as the basis for infringement by CJ's second later strain. But we need not reach Ajinomoto's contention that, in this circumstance, prosecution history estoppel does not apply at all, *i.e.*, that there is not even a presumed (though rebuttable) surrender of the asserted equivalent. The Commission did not so rule, instead concluding that the "tangential relation" exception applied, so that Ajinomoto did not surrender the protein produced by the codon-randomized non-*E. coli yddG* gene of CJ's second later strain. J.A. 41–44. We agree with that conclusion.[8]

In applying the "tangential relation" exception, we "ask[] whether the reason for the narrowing amendment was peripheral, or not directly relevant, to the alleged equivalent." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1369 (Fed. Cir. 2003). "[T]he inquiry into whether a patentee can rebut the *Festo*

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claims 9 and 15 as alternatives in the same way that original and amended claim 1 treated (A) and (B).

[8] CJ contends that Ajinomoto forfeited invocation of the "tangential relation" exception because it did not invoke the exception before the ALJ or in its request for review by the full Commission. CJ cites no authority that barred the Commission from exercising discretion to raise the issue and give the parties an adequate opportunity to address it, as the Commission did here.

presumption under the 'tangential' criterion focuses on the patentee's objectively apparent reason for the narrowing amendment." *Id.* Our cases require the patentee to show that the way in which the alleged equivalent departs from what the claim limitation literally requires is tangential to the discernible objective reason for the narrowing amendment. In that situation, there is no surrender of the equivalent by that amendment.

For instance, in *Insituform Technologies, Inc. v. CAT Contracting, Inc.*, the patent claimed a method of using a vacuum to impregnate a flexible tube with resin. 385 F.3d 1360, 1362–63 (Fed. Cir. 2004). The claims were originally rejected over a prior-art reference that disclosed a single vacuum source located far away from the resin source. *Id.* at 1369. The applicant amended the claim at issue to require a single vacuum source placed near the resin source. *See id.* at 1368–70. The alleged equivalent used multiple vacuum sources. *Id.* at 1369–70. We held that the "tangential relation" exception applied, observing that the purpose of the narrowing amendment was to distinguish the invention from the prior art based on the location of the vacuum source relative to the resin, not to limit the number of vacuum sources. *Id.* at 1370.

Similarly, in *Regents of the University of California v. Dakocytomation California, Inc.*, the patented method involved using DNA testing to detect chromosomal abnormalities. 517 F.3d 1364, 1369–70 (Fed. Cir. 2008). The claim at issue originally recited "disabling the hybridization capacity of repetitive sequences" generally. *Id.* at 1377. The examiner rejected the claim over several prior-art references, one of which disclosed disabling hybridization using unique sequence probes. *Id.* at 1378. In response, the applicants amended the claim to recite a particular technique of disabling hybridization using blocking nucleic acids. *Id.* The parties stipulated that the added "blocking nucleic acid" limitation was limited to human nucleic acids, but the alleged equivalent used synthetic

nucleic acids. *Id.* at 1376. We concluded that the narrowing amendment was tangential to how the equivalent differed from the literal claim limitation: "[I]n narrowing the claim to overcome the prior art rejections, the focus of the patentees' arguments centered on the method of blocking—not on the particular type of nucleic acid that could be used for blocking." *Id.* at 1378. Indeed, we noted, "the 'nucleic acid' limitation was never narrowed during prosecution and was not at issue in the office action rejecting the claims," and "none of the cited references concerned the type of nucleic acid that could perform the blocking, or mentioned the accused equivalent." *Id.*

Our decision in *Intervet Inc. v. Merial Ltd.* is to similar effect. In that case, the patent claimed DNA constructs encoding a type of porcine circovirus. 617 F.3d 1282, 1284 (Fed. Cir. 2010). The claim at issue originally recited DNA sequences from a group of thirteen open reading frames, which are portions of a gene that encode a protein. *Id.* at 1285–86, 1291. The examiner rejected the claim over open reading frames from another organism, noting that the claim as written could cover open reading frames from any organism. *Id.* at 1291. The applicants then amended the claim to require that the open reading frames be "of porcine circovirus type II." *Id.* The alleged equivalent was a nucleotide sequence that was over 99% homologous to one of the claimed sequences. *Id.* at 1286. The "tangential relation" exception applied to that equivalent, we held, because "[t]he rationale for the amendment was to narrow the claimed universe of [open reading frames] down to those of [porcine circovirus type II], and bore only a tangential relation to the question of which DNA sequences are and are not properly characterized as [porcine circovirus type II]." *Id.* at 1292.

This understanding of the "tangential relation" exception also underlies cases in which we have held that the patentee failed to establish that a narrowing amendment was tangential to the equivalent at issue. For example, in

Biagro Western Sales, Inc. v. Grow More, Inc., the claims at issue, which claimed buffered phosphorus fertilizers, were rejected over a prior-art reference disclosing a fertilizer that was buffered only when diluted. 423 F.3d 1296, 1299, 1306 (Fed. Cir. 2005). In response, the applicant amended the claims by adding the limitation "wherein said phosphorous-containing acid or salt thereof is present in an amount of about 30 to about 40 weight percent," explaining that the fertilizer must be concentrated and that the amendment specified a range for the concentration. *Id.* at 1305–06. The alleged equivalent contained phosphorus compounds at a concentration of between 59% and 62%. *Id.* at 1305. We concluded that the "tangential relation" exception did not apply, reasoning that it was "clear from the prosecution history that the reason for adding the range limitation was to overcome a prior art fertilizer that was not concentrated," and "both the reason for the amendment and the asserted equivalent relate to the concentration of the fertilizer." *Id.* at 1306.

Here, we conclude, the Commission correctly concluded that Ajinomoto had rebutted the *Festo* presumption because the amendment was tangential to the equivalent in question. The objectively evident rationale for the amendment was to limit the set of proteins within the claim's scope so that it no longer included the prior-art *E. coli* YfiK protein and, more generally, no longer allowed as wide a range of *amino acid* alterations (hence changes in the protein) as original alternative (B), which had allowed "deletion, substitution, insertion or addition of one or several amino acids in the amino acid sequence shown in SEQ ID NO: 2." J.A. 5047. The reason for the amendment had nothing to do with choosing among several DNA sequences in the redundant genetic code that correspond to the same protein. Indeed, it is undisputed that the non-*E. coli* YddG protein produced without codon randomization remains within the literal claim scope even after the amendment and that the non-*E. coli* YddG protein is identical whether

produced from the codon-randomized or the non-codon-randomized version of the non-*E. coli yddG* gene.

Accordingly, the reason for the narrowing amendment —limiting the amino-acid makeup of the proteins included in one of the alternatives covered by the claim—is unrelated to differences among the several DNA sequences that encode a given protein. Under *Festo*'s express provision for a "tangential relation" exception to the presumption as to the scope of surrender by amendment during prosecution, this conclusion about the reason for the amendment at issue does not "ignore[] how the patentee deliberately elected to narrow the claims" (Dissent at 6); rather, it identifies what was not within the "scope disclaimed" (*id.* at 7), so that it may be proved to infringe by satisfying the other requirements of the doctrine of equivalents. We therefore reject CJ's contention that prosecution history estoppel precludes the Commission's finding of infringement under the doctrine of equivalents for the second later strain.

2

CJ's second challenge to the Commission's finding regarding the protein limitation and CJ's second later strain is that the non-*E. coli* YddG protein of CJ's second later strain could not properly be found to be equivalent to the claimed *E. coli* YddG protein. Ajinomoto presented its equivalence case within the function-way-result framework, under which a product or process that does not literally satisfy a claim limitation may nevertheless infringe "if it performs substantially the same function in substantially the same way to obtain the same result." *Duncan Parking Techs., Inc. v. IPS Grp., Inc.*, 914 F.3d 1347, 1362 (Fed. Cir. 2019) (quoting *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608 (1950)). We conclude that substantial evidence supports the Commission's finding of equivalence under that test.

As to "function": Ajinomoto's expert, Dr. Gregory Stephanopoulos, testified that both *E. coli* and non-*E. coli*

YddG proteins function as "export protein[s] that actively export[] aromatic L-amino acids and aromatic L-amino acid analogs" out of the bacterial cell. J.A. 545–46. A 2007 article by Doroshenko et al. similarly explains that both proteins are involved in exporting aromatic compounds. *See* J.A. 9451. And Dr. So Young Kim, a CJ employee, testified during a deposition that both proteins would be expected to have similar functions based on similarities in the organisms from which they are derived. *See* J.A. 10641 ("Q. Based on the similarity between E. coli and [the non-*E. coli* organism], you would suspect that the protein coded by the [non-*E. coli*] yddG gene would be useful for whatever it does in E. coli, right? A. I think that way too."). Thus, the Commission's finding that both proteins perform the same function is supported by substantial evidence.

As to "way": Dr. Stephanopoulos testified that the two proteins are 85% to 95% identical in structure. J.A. 546. This range was corroborated by a 2002 article by Santiviago et al., which indicates an 85% structural identity, *see* J.A. 9444, and the Doroshenko article, which notes a 95% identity in amino-acid sequence, J.A. 9451. On the record here, substantial evidence supports a finding that the two proteins perform the membrane-transport function in substantially the same way. *See also Mylan Institutional LLC v. Aurobindo Pharma Ltd.*, 857 F.3d 858, 868 (Fed. Cir. 2017) (noting that the "function" and "way" inquiries often overlap or are synonymous).

As to "result": Dr. Stephanopoulos testified that, by exporting L-tryptophan out of the bacterial cell, both proteins increase the ability of bacteria to "produce and accumulate L-tryptophan." *See* J.A. 547. That statement is supported by CJ's fermentation data, which showed that strains containing the *E. coli yddG* gene but with a stronger promoter, and strains containing the non-*E. coli yddG* gene with a strong promoter, both showed greater production of L-tryptophan than did strains containing the *E. coli yddG* gene with the native promoter. *See* J.A. 7957; J.A. 10053. In

other words, enhancing the expression of either the *E. coli* or the non-*E. coli yddG* gene had the effect of increasing production of L-tryptophan, which supports an inference that the proteins encoded by those genes both result in increased L-tryptophan production. The Commission's findings regarding result are supported by substantial evidence.

CJ argues that the two proteins do not perform the same function in the same way because the *E. coli* YddG protein exports aromatic L-amino acids such as L-tryptophan, whereas the non-*E. coli* YddG protein exports a different compound—namely, paraquat (also known as methyl viologen). But a 2012 article by Liu et al. explains that YddG proteins can export both types of compounds. *See* J.A. 9751 ("YddG is classified as aromatic amino acid/paraquat exporter . . . ."). And Dr. Stephanopoulos, relying on the Santiviago article, testified that the non-*E. coli* YddG protein must be coupled to the OmpD protein, which is present in the non-*E. coli* organism but not *E. coli*, to export paraquat. J.A. 762 (citing J.A. 9439). The fact that the non-*E. coli* YddG protein may be involved in exporting compounds other than L-tryptophan in the non-*E. coli* organism does not undermine the Commission's well-supported finding that the non-*E. coli* YddG protein is involved in exporting L-tryptophan in the *E. coli* bacteria used by CJ.

B

CJ challenges the Commission's finding of infringement of *both* later strains on one additional ground. The Commission found that CJ's later strains met the resistance limitation. CJ argues that substantial evidence

does not exist to support that finding.[9] We reject that argument.

Several pieces of evidence indicate that, as a general matter, enhancing the activity of the YddG protein increases bacteria's resistance to L-tryptophan. Table 1 of the '655 patent shows that *E. coli* bacteria with multiple copies of the *yddG* gene introduced through plasmids demonstrated better growth on a tryptophan substrate, and thus more resistance, than unmodified *E. coli* bacteria. *See* '655 patent, col. 9, lines 50–65 (bottom row, compare column "pUC19" (-) with column "pYDDG1" (+)). Similarly, the Doroshenko article, mentioned above, describes an experiment in which *E. coli* bacteria with a stronger promoter preceding the *yddG* gene demonstrated enhanced resistance to L-tryptophan. *See* J.A. 9455 (row DV036, column DL-5-f-Trp).

CJ's fermentation data, mentioned above, also provides direct evidence that CJ's later strains have increased resistance to L-tryptophan. That data shows a greater volume of tryptophan with both of CJ's later strains than with unmodified *E. coli* bacteria. *See* J.A. 7957 (first later strain: middle table, row F4, column "Volume produced"); J.A. 10053 (second later strain: row "Product (g)" toward middle of table). Dr. Stephanopoulos indicated that a strain's ability to overproduce L-tryptophan necessarily meant that the strain had increased resistance to L-tryptophan. *See* J.A. 1448 ("[I]f that product feedback inhibits its own synthesis, clearly, this is not going to work."); *see also*

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[9] CJ does not challenge the finding that CJ's first later strain meets the protein limitation of the claim 15 alternative of claim 20. Specifically, CJ's first later strain uses a non-*E. coli yddG* gene without codon randomization, which hybridizes with the complement of SEQ ID NO:1 (*i.e.*, the nucleotide sequence of the *E. coli yddG* gene), and thus falls within the literal scope of claim 15.

J.A. 521 (stating that bacteria that "exhibit enhanced resistance to an aromatic L-amino acid or an aromatic L-amino acid analog" also "overproduce the corresponding aromatic L-amino acid analog").

CJ's objections to the sufficiency or even relevance of this evidence are unpersuasive. CJ points out that the bacteria used to generate the data in Table 1 of the '655 patent contained plasmids with more than the two copies of the *yddG* gene in CJ's later strains. *See* J.A. 1229. The Doroshenko article, however, indicates that enhancing the activity of even a single copy of the *yddG* gene can increase resistance to L-tryptophan. CJ responds that the strain studied in Doroshenko used a strong λP_L promoter, while CJ's later strains use relatively weaker non-*E. coli* native *yddG*, *rmf*, and *rhtB* promoters. *See* J.A. 9454. But Dr. Stephanopoulos testified that at least the *rmf* promoter in both of CJ's later strains also is more potent than the native *E. coli yddG* promoter. J.A. 554. Thus, even if CJ is correct that its later strains do not contain tandem promoters, the Commission could reasonably infer that the promoters used in CJ's later strains enhance the activity of the *yddG* genes relative to unmodified *E. coli* bacteria and thereby increase those strains' resistance to L-tryptophan.

CJ also cites Ajinomoto's 2002 Progress Report as evidence that enhancing a single copy of the *yddG* gene is insufficient to enhance resistance to L-tryptophan. That report states that an experiment using "only one copy" of the *yddG* gene with a P_L promoter "does not correctly model[]" an earlier experiment using a "moderate-copy-number" plasmid with the *yddG* gene, which had shown a "positive effect" of the *yddG* gene on tryptophan production. J.A. 10268. No more need be inferred from the report than that enhancing a single copy of the *yddG* gene increases resistance to L-tryptophan less than using a greater number of copies. The Commission did not need to infer that enhancing a single copy as in CJ's later strains does not enhance resistance at all.

Further, CJ asserts that the increased production of L-tryptophan, and thus the enhanced resistance to L-tryptophan, observed in its later strains could be attributable to the presence of other genetic mutations rather than to increased YddG protein activity alone. *See* J.A. 442. But the claims require only that the protein "has the activity to make the bacterium resistant" to L-tryptophan, not that the protein be the sole cause of the bacterium's enhanced resistance to L-tryptophan. *See* '655 patent, col. 22, lines 57–59. Considering the already-mentioned evidence that the YddG protein generally has the effect of increasing resistance to L-tryptophan, the Commission had substantial evidence from which to find that it was more likely than not that increased activity of the YddG protein at least partly contributed to the enhanced resistance of CJ's later strains.

C

CJ's final contention in its cross-appeal seeks reversal of the Commission's rejection of CJ's invalidity challenge to claim 20. CJ argues that substantial evidence does not support the Commission's finding that CJ did not prove lack of an adequate written description for the genus of "more potent promoter[s]" recited in claims 9 and 15 and, by incorporation, in claim 20. We reject CJ's argument.

"[A] sufficient description of a genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010) (en banc). The Commission found both that the '655 patent discloses a representative number of species of more potent promoters and that there are structural features common to the genus of more potent promoters. Both of those findings are supported by

substantial evidence, and they suffice to uphold the Commission's rejection of CJ's written-description challenge.

1

As to a representative number of species, we have recognized that the amount of disclosure necessary to satisfy the written-description requirement "will necessarily vary depending on the context," considering such facts as "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology," and "the predictability of the aspect at issue." *Ariad*, 598 F.3d at 1351 (quoting *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005)). In some circumstances, we have added, "a patentee may rely on information that is 'well-known in the art' for purposes of meeting the written description requirement," because "the specification is viewed from the perspective of one of skill" in the relevant art. *Bos. Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366 (Fed. Cir. 2011).

The '655 patent discloses four examples of "potent promoters": "P_L promoter of lambda phage," the "lac promoter," the "trp promoter," and the "trc promoter." '655 patent, col. 6, lines 21–24. The patent also cites the 1986 article by Deuschle et al. as disclosing "examples of potent promoters" and "[m]ethods for [the] evaluation [of] the strength of promoter[s]." *Id.*, col. 6, lines 16–21. That article provides data about the relative strength of fourteen promoters and describes a general methodology for determining promoter strength in *E. coli* bacteria. J.A. 6174–77. This evidence supports the Commission's finding that "enhancing promoter activity was well-known" and that a skilled artisan "would have been able to identify more potent promoters by employing common tools for measuring RNA transcription." J.A. 46.

The '655 patent also makes clear that its invention was "identifying the yddG gene encoding a membrane protein" and discovering that the gene "conferred on a

microorganism resistance to phenylalanine and several amino acid analogues" when the gene was amplified or its expression enhanced, *see* '655 patent, col. 2, lines 46–57, not the well-known techniques for performing the amplification or expression enhancement, *see id.*, col. 5, line 57, through col. 6, line 33. We have explained that the representative-species inquiry is directed to whether the inventor "has truly invented the genus" as opposed to "a research plan, leaving it to others to explore the unknown contours of the claimed genus." *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1300 (Fed. Cir. 2014). Here, the genus of more potent promoters was already well explored in the relevant art by the time of the '655 patent's invention. In these circumstances, the Commission permissibly found in the specification, read in light of the background knowledge in the art, a representative number of species for the genus of more potent promoters.

2

As to a common structural feature, the Commission found that a skilled artisan could "identify more potent *yddG* promoters given the well-known link between consensus sequence and promoter strength," *i.e.*, that promoters having fewer departures from a "consensus sequence" in a promoter are generally stronger than promoters with more departures from such a sequence. J.A. 46.[10] Substantial evidence supports that finding. For instance, a 1983 article by Hawley and McClure describes a study demonstrating that most "mutations that decrease initiation frequency also decrease the homology of the promoter to the consensus sequence, while up-mutations increase the

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[10] The consensus sequence is a specific nucleotide sequence that appears in the promoters associated with many different genes in the genome of a particular organism. In *E. coli*, the consensus sequence has two parts: TTGACA at the -35 region and TATAAT at the -10 region.

homology in" most instances. J.A. 6237. Similarly, a 1986 article by Horwitz and Loeb explains that "mutations that increase transcription, 'up mutations,' usually increase homology with the consensus sequence and spacing," while "mutations that decrease transcription, 'down mutations,' usually decrease homology with the consensus sequence and spacing." J.A. 6251.

CJ disputes that similarity to the consensus sequence defines a common structural feature, citing several articles as indicating that a promoter closer to the consensus sequence will not always be stronger than one farther from that sequence. For instance, a 1998 article by Jensen and Hammer reports that a pattern observed in another organism—that "the relatively strong promoters were the perfect ones," *i.e.*, those closer to the consensus sequence—"did not hold true for *E. coli*: here the promoters which had either an error in the consensus sequence or a shorter spacer were relatively strong." J.A. 9149. Moreover, a 1985 article by Aoyama and Takanami states that similarity to the consensus sequence "is still not enough to predict the site and strength of promoter from a given sequence," J.A. 6215, and a 1999 book edited by Fernandez and Hoeffler notes that "the strongest promoters in *E. coli* do not necessarily adhere to the consensus sequence," J.A. 9113.

CJ's argument both assumes too strict a legal standard and reads too much into its cited references. Adequate written description does not require a perfect correspondence between the members of the genus and the asserted common structural feature; for a functionally defined genus like the one at issue here, we have spoken more modestly of a "*correlation* between structure and function." *Ariad*, 598 F.3d at 1350 (emphasis added). In any event, CJ's evidence at most establishes that, starting with the consensus sequence, deviations from that sequence do not *always* decrease promoter strength, at least in *E. coli*. But the genus at issue here is "more potent promoter[s]" than the native promoter, not less potent promoters than the

consensus sequence. And the Commission had substantial evidence from which to find that, starting from the native *E. coli yddG* promoter, deviations toward the consensus sequence generally increase promoter strength.

The cases cited by CJ in which we have held genus claims to lack an adequate written description are inapposite. In *Boston Scientific*, the specification contained "no examples of macrocyclic lactone analogs of rapamycin" (the claimed genus) and essentially "no guidance on how to properly determine whether a compound is a macrocyclic lactone analog of rapamycin." 647 F.3d at 1364. In *AbbVie*, there was "no evidence to show any described antibody to be structurally similar to, and thus representative of," an antibody accused of coming within the claim, nor was there "evidence to show whether one of skill in the art could make predictable changes to the described antibodies to arrive at other types of antibodies such as" the accused antibody. 759 F.3d at 1301. And in *Regents of the University of California v. Eli Lilly & Co.*, the specification described "a process for obtaining human insulin-encoding cDNA" (such cDNA required by the claim at issue) but not any "sequence information indicating which nucleotides constitute human cDNA" or "further information in the patent pertaining to that cDNA's relevant structural or physical characteristics." 119 F.3d 1559, 1567 (Fed. Cir. 1997). Here, by contrast, the '655 patent expressly provides four examples of "more potent promoters," and the Commission supportably found that a skilled artisan could make relatively predictable changes to the native promoter to arrive at a more potent promoter.

IV

For the foregoing reasons, we affirm the Commission's decision.

No costs.

AFFIRMED

United States Court of Appeals for the Federal Circuit

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AJINOMOTO CO., INC., AJINOMOTO HEARTLAND INC.,
Appellants

v.

INTERNATIONAL TRADE COMMISSION,
Appellee

CJ CHEILJEDANG CORP., CJ AMERICA, INC., PT CHEIJEDANG INDONESIA,
Intervenors

- -

CJ CHEILJEDANG CORP., CJ AMERICA, INC., PT CHEIJEDANG INDONESIA,
Appellants

v.

INTERNATIONAL TRADE COMMISSION,
Appellee

AJINOMOTO CO., INC., AJINOMOTO HEARTLAND INC.,
Intervenors

____

2018-1590, 2018-1629

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Appeals from the United States International Trade Commission in Investigation No. 337-TA-1005.

DYK, *Circuit Judge*, concurring-in-part and dissenting-in-part.

I join the majority as to parts I, II, III (B) (as it relates to Strain A, corresponding to the "first later strain" in the majority) and (C). I respectfully dissent from the majority's conclusion that Ajinomoto successfully rebutted the presumption of prosecution history estoppel under the tangential exception as to respondent's recombinant bacterial Strain B, which corresponds to the "second later strain" referred to by the majority, *see* Majority Op. at 15.

On appeal, the only asserted claim is claim 20 of U.S. Patent No. 7,666,655 ('655 patent). It covers "[a] method for producing an [amino acid,] which comprises cultivating the bacterium according to any one of claims 9[, or 15]." '655 patent, col. 24, ll. 4–6. In relevant part, claim 9 covers a recombinant bacteria having a "protein consist[ing] of the amino acid sequence of SEQ ID NO: 2." *Id*. col. 22, ll. 56–57. This corresponds to the amino acid sequence of *E. coli* YddG protein (a membrane-bound protein involved in the cellular export of aromatic amino acids). Strain B does not literally infringe claim 9 because it produces a protein with an amino acid sequence that differs from SEQ ID NO: 2. *See* J.A. 37. Instead, Ajinomoto asserts infringement under the doctrine of equivalents, arguing that Strain B's non-*E. coli* YddG protein is equivalent to the *E. coli* YddG protein (SEQ ID NO: 2) in claim 9.

The prosecution history shows that claim language was amended such that the accused equivalent is excluded.[1]

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[1] Everyone agrees that the relevant prosecution history for the analysis focuses on the language in claim 1,

Originally, the claim language covered variations of SEQ ID NO: 2, stating that it covered "deletion, substitution, insertion or addition of one or several amino acids" of SEQ ID NO: 2. J.A. 5609. During prosecution, the examiner rejected the claim as anticipated by prior art (Livshits) that disclosed a recombinant *E. coli* bacteria producing YfiK protein, encoded by the *yfiK* gene, which had an amino acid sequence different from the SEQ ID NO: 2 but still satisfied the claim limitations. J.A. 5378. Specifically, the examiner stated "Livshits et al. anticipate claims 1-4 because the *yfiK* gene product can be considered a protein" meeting the claim limitation above. *Id.* In response to this rejection, the patentee narrowed the claim language (which now appears in claim 15) to only cover protein variants differing from SEQ ID NO: 2 when they are "encoded by a nucleotide sequence that hybridizes with the nucleotide sequence of SEQ ID NO: 1[, the *E. coli yddG* gene,] under stringent conditions comprising 60°C, 1 x SSC, 0.1% SDS." J.A. 5609; *see* '655 patent, col. 23, ll. 19–22.[2] The patentee stated that "[i]n view of this amendment, Livshits et al no longer anticipates the claimed invention." J.A. 5617.

The majority assumes that prosecution history estoppel presumptively applies in this case. Majority Op. at 18. But the majority concludes that Ajinomoto is still not precluded from arguing infringement under the doctrine of equivalents based on the tangential exception.

We have consistently described this exception as "very narrow." *Integrated Tech. Corp. v. Rudolph Techs., Inc.*, 734 F.3d 1352, 1358 (Fed. Cir. 2013) (quoting *Cross Med.*

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which was later utilized in claims 9 and 15 that were added later in prosecution.

[2] Strain B does not literally infringe claim 15 because the non-*E. coli* YddG protein's encoding nucleotide sequence does not hybridize with SEQ ID NO: 1 under the claimed conditions.

Prods., Inc. v. Medtronic Sofamor Danek, Inc., 480 F.3d 1335, 1342 (Fed. Cir. 2007)). Under this exception, the question is "whether the reason for the narrowing amendment was peripheral, or not directly relevant, to the alleged equivalent." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1369 (Fed. Cir. 2003) (en banc). The inquiry "focuses on the patentee's objectively apparent reason for the narrowing amendment," which "should be discernible from the prosecution history record." *Id.* (emphasis added). In my view the "reason for the narrowing amendment" in this case is directly related to the equivalent.

Originally, the claim covered proteins with amino acid sequence variations from SEQ ID NO: 2, which would have included the non-*E. coli* YddG protein at issue here. The examiner rejected the original claim based on anticipating prior art, and the patentee responded with a narrowing amendment. Instead of continuing to define the covered proteins in terms of amino acid sequence variations from SEQ ID NO: 2,[3] the patentee deliberately chose to redefine the claimed proteins in terms of the ability of their encoding nucleotide sequences to hybridize with SEQ ID NO: 1 under the claimed conditions. The amended claim language excluded the prior art protein (Livshits) because it was made based on a nucleotide sequence that did not meet the newly added hybridization requirement. The accused equivalent is similarly not covered by the amended claims because it is produced based on an encoding nucleotide sequence that does not hybridize with SEQ ID NO: 1 under the claimed conditions. Thus, I do not see how the reason

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[3] The patentee later added claim language that covered other, more limited, variations from the amino acid sequence of SEQ ID NO: 2, by "one to five amino acids," but that claim language is not at issue here. '655 Patent, col. 21, l. 42.

for the narrowing amendment is tangential to the accused equivalent.

Ajinomoto argues that "[t]o the extent anything was given up during prosecution, it was the YfiK protein [disclosed in Livshits] . . . and, possibly, other non-YddG proteins." Ajinomoto Response & Reply Br. at 41 (emphasis omitted). Ajinomoto's argument that prosecution history estoppel would only apply to the specific prior art protein (or possibly other non-YddG proteins) is not only inconsistent with how the patentee amended the claims but also our caselaw. Specifically, "[Ajinomoto's] representations convey to the public that it was relying on [the claimed hybridization requirement] to overcome the prior art. The public is entitled to rely on those representations." *Integrated Tech.*, 734 F.3d at 1359. "The fact that the inventors may have thought after the fact that they could have relied on other distinctions in order to defend their claims[, e.g., by limiting the claim to only YddG-type proteins,] is irrelevant and speculative . . . ." *Schwarz Pharma, Inc. v. Paddock Labs., Inc.*, 504 F.3d 1371, 1377 (Fed. Cir. 2007). "It is not relevant to the determination of the scope of the surrender that the applicant did not need to amend the claims" in the way that it chose to do so "in order to overcome the prior art." *Lucent Techs., Inc. v. Gateway*, 525 F.3d 1200, 1218 (Fed. Cir. 2008) (citing *Norian Corp v. Stryker Corp.*, 432 F.3d 1356, 1361–62 (Fed. Cir. 2005)).

The majority adopts a slightly different version of Ajinomoto's untenable argument. The majority concludes that the "objectively evident rationale" for the narrowing amendment was "to limit the set of proteins within the claim's scope so that it no longer included the prior-art [protein], and, more generally, no longer allowed as wide a range of *amino acid* alterations." Majority Op. at 21 (emphasis in original). The majority reasons that because Strain A, which makes the same protein as Strain B but with a different nucleotide sequence, literally infringes claim 15, somehow Strain B should be found to infringe

claim 9 under the doctrine of equivalents. It theorizes that "[t]he reason for the amendment had nothing to do with choosing among several DNA sequences in the redundant genetic code that correspond to the same protein" (i.e., the accused equivalent). *Id.* at 21. In this way, the majority concludes that the reason for the narrowing amendment—limiting the range of proteins covered by the claim—is unrelated to the way in which the equivalent departs from the literal claim limitation—differences among the several DNA sequences that encode a given protein.

The problem with the majority's analysis is that it ignores how the patentee deliberately elected to narrow the claims. The anticipating prior art disclosed *E. coli* YfiK protein, encoded by the *yfiK* gene, and this prior art was avoided by narrowing the claim to only cover certain encoding nucleotide sequences. That rationale is directly related to the accused equivalent, which does not infringe because it does not use a covered encoding nucleotide sequence. In other words, the rationale for the narrowing amendment (avoiding a prior art protein based on its encoding nucleotide sequence that does not meet the newly claimed hybridization requirement) directly relates to the accused equivalent (a protein made by an encoding nucleotide sequence that does not meet the newly claimed hybridization requirement).

The cases cited by the majority also do not support its approach. In *Insituform Technologies, Inc. v. CAT Contracting, Inc.*, 385 F.3d 1360 (Fed. Cir. 2004), and *Regents of the University of California v. Dakocytomation California*, 517 F.3d 1364 (Fed. Cir. 2008), multiple limitations were added with a narrowing amendment but only one of those limitations related to what was taught in the prior art cited by the examiner. We held that the equivalent to the other limitation was permitted under the tangential exception. In *Insituform*, the rationale for the amendment was to limit the location of the vacuum source, not the number of vacuum sources (the accused equivalent). 385 F.3d

at 1370. In *Regents*, the rationale for the amendment was to limit the type of blocking method, not the particular types of nucleic acids that could be used in that method (the accused equivalent). 517 F.3d at 1378. These cases cannot be read as allowing the patentee to recapture scope disclaimed in order to distinguish the prior art, which is exactly what the patentee is attempting to do here. The anticipating prior art cited by the examiner specifically taught a protein made by a particular gene, and the patentee narrowed the claim to avoid this prior art by limiting the claim to only cover proteins made by particular nucleotide sequences (which neither the prior art nor Strain B have).

Our decision in *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282 (Fed. Cir. 2010), is also inapposite. There, the claims were "narrow[ed from] the claimed universe of [nucleotide sequences] down to those of [porcine circovirus type II ('PCV-2')]," but there remained the tangential "question of which DNA sequences are and are not <u>properly characterized as PCV-2</u>." *Id.* at 1292 (emphasis added). In contrast, there is no question here of which nucleotide sequences are "properly characterized" as being included under the claim language—only those that hybridize with SEQ ID NO: 1 "under stringent conditions comprising 60°C, 1 x SSC, 0.1% SDS" are covered. J.A. 5609. There is no dispute that CJ's bacterial strain does not satisfy this specific and unambiguous limitation.

In my view the tangential exception cannot apply. The equivalent is directly related to the reason for the amendment—to exclude those proteins made by an encoding nucleotide sequence that does not hybridize with SEQ ID NO: 1 under the specified conditions. I respectfully dissent from the majority's contrary conclusion.